REMARKS

The foregoing amendment proposes to amend claim 1 in order to obviate the rejection of certain claims over the Plank article, to revise the cross-reference paragraph in order to claim CIP status from an another earlier filed application, and to make certain amendments in the Written Description in order to obviate rejections under 35 U.S.C. § 112.

Defective Declaration

In paragraph 2 of the Office Action, the Examiner notes that the supplemental declaration submitted in accordance with Rule 67(a) is defective. There appear to be two reasons for the Examiner's view.

The first defect noted by the Examiner is that the declaration apparently does not acknowledge the duty to disclose to the Patent and Trademark Office all information known to the person to be material to patentability which occurred between the filing date of the prior application and the filing date of the continuation-in-part application referred to in the declaration. Applicants respectfully point out, however, that this language is contained in the declaration.

The second defect is that the declaration previously submitted referred to amendments that contain new matter and this is contrary to MPEP § 602. The alleged new matter involved amendments to claims 34-37. However, in the June 2003 Amendment, these claims were cancelled. Therefore, it is believed that the issue of new matter no longer exists and that, in these circumstances, the declaration was a proper declaration.

Nevertheless, Applicants are complying with the Examiner's requirement to submit another supplemental declaration. A further reason for doing so is that Applicants

are now claiming priority from another earlier filed application and therefore another Supplemental Declaration under Rule 67(a) would be required in any event. This declaration is currently being prepared and will be submitted in due course. Meanwhile, Applicants are enclosing an unexecuted copy. It should be noted that this declaration makes no reference to any amendments.

Inventor McBride has now signed the declaration that was submitted in June 2003. In order to complete the record in the PTO file, this declaration is now enclosed.

Objections to the Disclosure

In paragraph 4 of the Office Action, the Examiner has objected to the disclosure because of certain informalities. These have now been corrected in paragraphs 2, 3, and 4 of the foregoing "Amendments to the Written Description". With respect to the change of periods to commas before "Hcy" in the list on page 12 and in the Table on page 19, it is believed that this occurred when the application, which had been prepared at a different firm, was scanned into the Fish & Richardson system. There was no intention to make any changes.

Double Patenting Rejection

In paragraph 5 of the Office Action, the Examiner has maintained the double patenting rejection for claims 1-3, 6-8, 11-17, 19 and 38. A Terminal Disclaimer was submitted in June 2003 but was, inadvertently, unsigned. A signed version of the Terminal Disclaimer is now enclosed. Any inconvenience caused by the previous omission of the signature is regretted.

Effective Filing Date for the Claims of this Application

In paragraph 6 of the Office Action, the Examiner reasserts his ruling that the effective filing date for all of the claims of this application is deemed to be 2 May 1994, the filing date of the instant application, rather than the filing date of parent application No. 07/807,062, now U.S. Patent No. 5,443,815 ("Dean '815"). Applicants are not questioning the availability of Dean '815 as available prior art under 35 U.S.C. § 102(e), but the issue involved in the rejection of certain of Applicants' claims over Dean '815 – discussed in more detail below – concerns the extent to which Dean '815 represents an invention "by another".

A similar situation exists with respect to U.S. Patent No. 5,849,260 (Dean '260"). Dean '260 issued on an application (No. 08/273,274 filed 11 July 1994) that was a continuation of application No. 07/886,752 filed on 21 May 1992. A review of the specification of Dean '260 and of application No.07/886,752 reveals that the instant application is, in fact, a CIP of application No. 07/886,752. This matter will be discussed below in further detail, in connection with the Examiner's rejection of certain claims under 35 U.S.C. § 102(e) as anticipated by Dean '260. Applicants are not asserting that Dean '260 is not available prior but, here again, the issue turns on the question of whether we have an invention "by another".

With respect to correcting the "related U.S. application data" in Dean '260, the assignee is currently preparing a request for a certificate of correction under 37 C.F.R. § 1.323.

Rejection over Dean U.S. Patent No. 5,443,815

In paragraph 8 of the Office Action, the Examiner has finally rejected certain claims under 35 U.S.C. § 102(e) as anticipated by Dean '815.

> Claims 1-3, 6-8, 11-17, 19 and 38 are rejected under 35 U.S.C. § 102(e) as being anticipated by Dean et al. (U.S. Patent No. 5,443,815). Dean et al. '815 teaches specific peptides in Table I which comprise a specific binding compound (e.g., the GRGD of SEQ ID NOS:2 and 3 or the RALVDTLK of SEQ ID NO:4) and a radiolabel complexing moiety (e.g., the GGC or SEQ ID NO:2 or the maGGG and PenGGG of SEQ ID NOS:3-4). The peptides are labeled with Tc-99m (see Example 2). More generally, the peptides can be labeled by incubation of the peptide in the presence of a stannous chloride reducing agent, and a kit can be provided for preparing the radiolabeled peptide by a reduction method. See, e.g., column 4, line 45 – column 5, line 5. With respect to claims 11-13, note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art. The radiolabeled peptides are used for imaging a mammalian body (see, e.g., the Abstract and column 5, lines 13-43).

A substantially identical rejection was made in the December 2002 Office Action and, in their June 2003 response, Applicants filed a Declaration under 37 C.F.R. § 1.132 from inventor Dean. The Examiner commented on Applicants' response as follows:

> The rejection under 35 U.S.C. 102(a) based upon Dean et al. (U.S. Patent No. 5,443,815) is maintained. The declaration by Inventor Dean filed July 28, 2003 does not overcome the rejection because it does not show that the subject matter of the reference relied upon in the rejection is not "by another". The declaration states that certain subject matter was conceived by Inventor Dean (see paragraph 4 of the declaration). However, the inventorship of the instant application is Inventor Dean plus Inventors Lister-James and McBride. This still constitutes "by another". See MPEP 2136.04 for a discussion of the meaning of the statutory phrase "by another". For analogous reasons, the rejection over the WO Patent Application 93/10747 is also maintained.

Reconsideration of this rejection is respectfully requested. The issue here is whether, in the circumstances of the present case, Dean '815 discloses an invention "by another".

The examiner cites MPEP 2136.04 to show what the Patent and Trademark Office regards as "another" within the meaning of 35 U.S.C. § 102(e). The leading case is In re Land, 368 F.2d 866, 151 U.S.P.Q. 621 (C.C.P.A. 1966) which holds that "another" is simply another inventive entity. Thus, if an application has inventor A and a cited reference has inventors A + B (or vice versa), the reference derives from an application filed "by another". However, although the Land decision has never been overruled, the Federal Circuit has been narrowly construing this concept where the application and the

cited reference have an inventor in common. Thus, in Applied Materials Inc. v. Gemini Research Corp., 835 F.2d 279, 15 U.S.P.Q.2d 1816 (Fed. Cir. 1988), the court stated:

> The fact that an application has named a different inventive entity than a patent does not necessarily make that patent prior art.

This statement is quoted in MPEP 2136.05. A recent decision addressing this question is Purdue Pharma L.P. v. Boehinger Ingelheim GmbH, 98 F. Supp. 2d 362, 55 U.S.P.Q.2d 1168 (S.D.N.Y. 2000), *aff'd* 237 F.3d 1359, 57 U.S.P.Q.2d 1647 (Fed. Cir. 2001), in which the District Court said:

> Applied Materials holds that if a parent patent fully discloses an invention that in fact is the work of an overlapping inventive entity and that is claimed in a continuing application listing that entity, then the presence of that subject matter in the earlier patent indicates that the present invention was already in existence as of the filing date of the parent application. And on that rationale, the invention disclosed in the earlier patent does not constitute prior art capable of anticipating the present invention.

55 U.S.P.Q.2d at 1181.

Applicants are not asserting that the claims in the instant application are entitled to the filing date of Dean '815. However, the alleged anticipatory subject matter in Dean '815 was, in fact, the work of Dr. Dean and therefore that portion of the invention disclosed in the earlier patent does not constitute prior art within the meaning of 35 U.S.C. § 102(e).

Rejection over WO 93/10747

In paragraph 9 of the Office Action, the Examiner is finally rejecting certain claims under 35 U.S.C. § 102(a) as anticipated by PCT Publication WO 93/10747 ("WO '747").

> Claims 1-3, 6-8, 11-17, 19, and 38 are rejected under 35 U.S.C. 102(a) as being anticipated by the WO Patent Application 93/10747. The WO Patent Application '747 contains the same disclosure as Dean et al. (U.S. Patent No. 5,443,815) applied above, and anticipates the claims for the same reasons set forth above.

The Examiner and Applicants agree that WO '747 contains substantially the same disclosure as Dean '815. In view of the previously submitted Declaration from Dr. Dean and the foregoing discussion with respect to Dean '815, it is urged that this rejection be withdrawn.

Rejection over Dean U.S. Patent No. 5,849,260

In paragraph 10 of the Office Action, all of the claims in this application, except claim 21, have been rejected under 35 U.S.C. § 102(e) as anticipated by Dean '260.

> Claims 1-3, 6-8, 11-17, 19, 20, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al. (U.S. Patent No. 5,849,260). Dean et al. '260 teaches specific peptides in the Table at columns 11-12 which comprise a specific binding compound and a radiolabel complexing moiety. The peptides are labeled with Tc-99m, either through use of a stannous chloride reducing agent or through ligand exchange, and kits for preparing the radiolabeled peptides are provided. The peptides are used to image thrombus sites in a mammalian body. See, e.g., the Abstract; column 9, lines 14-46; and Example 2. The Table teaches peptides GRGDGGC, maGGRGDF, mmpGGGRGDF, and GRGDGGGGC in which the GGC, maGG, mmpGGG, and GGGC residues, respectively, correspond to Applicants' radiolabel complexing moiety and the remaining residues correspond to Applicants' specific binding compound. Dean et al. '260 also teaches, e.g., the fourth compound of the Table, in which the C-terminal GCamide residues correspond to a peptide comprising 2 amino acids attached to the carbonyl group of Applicants' Z residue, the GGGC residues correspond to Applicants' radiolabel complexing moiety of formula I, and the remainder of the compound corresponds to Applicants' specific binding compound. Note that applicants' claims do not contain any limitations which exclude amino acids containing a thiol group from forming part of, e.g., the specific binding compound, the amino acid or peptide attached to the carbonyl group of Z, or the one or more amino acids which can link the peptide and the moiety.

In the June 2003 response, Applicants noted that the inventorship of Dean '260 is Dean + Lister-James, whilst the inventorship of the instant application is Dean + Lister-James + McBride. Applicants urge that, in these circumstances, Dean '260 does not represent an invention "by another" within the meaning of 35 U.S.C. § 102(e). The Examiner maintained his rejection over Dean '260, commenting (page 12 of the Office Action) that

Dean '260 represents "by another" and cites MPEP 2136.04. Reconsideration of the rejection is respectfully requested.

In his rejection, the Examiner points to the Table in column 12 of Dean '260 and notes in four specifically disclosed peptides, asserting that the residues –GGC, maGG-, mmpGG- and –GGGC correspond to Applicants' radiolabel complexing moiety. On further review of this rejection, it appears that the instant application is, in fact, a continuation-in-part of application No. 07/886,752 filed 21 May 1992, of which Dean '260 is a continuation. Applicants are therefore proposing to amend the cross-reference paragraph. Applicants will also, in due course, file an appropriate substitute declaration under 37 C.F.R. § 1.67(a). The peptides GRGDGGC and GRGDGGGGC are disclosed in the instant application at page 12, lines 25 and 27, respectively. 2-Mercaptpacetic acid and 3-Mercaptopropionic acid are among the amino acids conforming to the definition of (mercaptocarboxylic acid) as set forth at page 9, line 10.

The attention of the Examiner is respectfully directed to the declaration of Dr. Dean that was submitted with the June 2003 response. The declaration shows that the subject matter of Dean '260 relied upon the Examiner was conceived by inventor Dean. The pages attached to said Declaration are from a laboratory notebook identified as "RTD-1", and specifically constitute pages 1, 2, 3, 4, 161 and 162. Pages 1 and 2, dated 11 April 1990, show a composition identified as No. 1 as being a reagent comprising a specific binding compound "peptide" and a radiolabel complexing moiety which is -GGC, as shown in Dean '260. Page 3 of the notebook, also dated 11 April 1990, identifies a compound No. 2 showing the radiolabel complexing moiety maGG- as disclosed in Dean '260. Radiolabel complexing moieties comprising the -GRGD peptide are shown on page 4, under nos. 4, 5 and 6. Page 161 also shows a specific binding compound GRGD peptide sequence.

Under the circumstances, the invention disclosed in Dean '260 cannot be regarded as prior art capable of anticipating Applicants' claims.

Rejection over WO 93/17719

In paragraph 11 of the Office Action, all of the claims, except for claim 20, were rejected under 35 U.S.C. § 102(a) as anticipated by PCT publication WO 93/17719 ("WO '719").

> Claims 1-3, 6-8, 11-17, 19, 21 and 38 are rejected under 35 U.S.C. 102(a) as being anticipated by the WO Patent Application 93/17719. The WO Patent Application '719 teaches specific peptides at pages 20-22 and 24 which comprise a specific binding compound and a radiolabel complexing moiety. The peptides are labeled with Tc-99m, either through use of a dithionate, stannous, or ferrous reducing agent or through ligand exchange, and kits for preparing the radiolabeled peptides are provided (see, e.g., page 14, line 24-15, line 6). The peptides are used to visualize sites in inflammation, including abscesses and sites of occult infection (see, e.g., the Abstract and page 16, lines 9). With respect to the peptide, e.g., at page 20, line 17, of the WO Patent Application '719, the residues $(VGVAPG)_3$ correspond to Applicants' specific binding compound (see also page 12, line &); the residues GGGC correspond to Applicants' radiolabel complexing moiety of formula I; and the residues GCamide correspond to a peptide comprising 2 amino acids lined to the carbonyl group of Applicants' Z.

In the June 2003 response, Applicants attempted to overcome this rejection by submitting a declaration from inventor Lister-James. (The declaration was originally submitted in unexecuted form but a fully executed version was filed on 28 July 2003.) The Examiner accepted the Lister-James declaration as a partial response only.

> The rejection based upon the WO Patent Application 93/17719 is maintained. Once the executed declaration by Lister-James is submitted, the examiner will accept its statements with respect to peptides comprising a CGC motif, i.e. the examiner will not argue that such peptides anticipate the instant claims. However, the WO Patent Application '719 teaches peptides which comprise a GGC or a CGG motif and which do not comprise a CGC motif. See, e.g., page 21, lines 3 and 5, and page 24, line 4. These peptides will continue to anticipate Applicants' claims.

Reconsideration of this rejection is respectfully requested.

In maintaining this rejection, the Examiner has pointed to the GGC and CGG motifs disclosed at page 21, lines 3 and 5, and at page 24, line 4. In the June 2003 response, Applicants should have pointed out that these motifs were included in the notebook pages attached to the Declaration of Dr. Dean; Applicants apologize for this omission.

Turning now to the Dean Declaration, it is noted that the GGC motif is set forth on page 4 of the attached notebook pages and that the CGG motif is set forth on pages 3 and 4.

The situation here therefore is very similar to the situation as regards Dean '815 and Dean '260. Although this rejection under discussion was made under § 102(a) rather than § 102(e), the rationale of the Applied Materials case is equally applicable. The inventors in WO '719 are Dean + Lees + Buttram + Lister-James. The Dean Declaration shows unequivocally that the peptides comprising the GGC and CGG motifs were part of the contribution to the invention made by Dr. Dean. Therefore, WO '719 does not anticipate the claims of the instant application.

Rejection over Dean U.S. Patent No. 6,017,510

In paragraph 12 of the Office Action, the Examiner is rejecting all of the claims, except for claim 20, under 35 U.S.C. § 102(e) as anticipated by Dean U.S. Patent No. 6,017,510 ("Dean '510").

> Claims 1-3, 6-8, 11-17, 19, 21, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al. (U.S. Patent No. 6,017,510). Dean et al. '510 is the U.S. equivalent of the WO Patent Application '747 applied above, and anticipates the claims for the same reasons set forth above.

In the June 2003 response, Applicants traversed this rejection, pointing out that the Lister-James declaration in connection with the rejection based on WO '719 is also effective against the rejection based on Dean '510. The Examiner's response was

> The rejection based upon Dean et al. (U.S. Patent No. 6,017,510) is maintained for the same reasons set forth above with respect to the WO Patent Application '719. Applicants are correct that Dean et al. '510 is the equivalent of the WO Patent Application '719 rather than the WO Patent Application 747. The examiner apologizes for any confusion this error may be caused.

There is some understandable confusion here regarding WO '719 and its American equivalent. The equivalent of WO '719 is Dean U.S. Patent No. 5,989,519, which is a CIP of Dean '510 in that it contains additional subject matter. Dean '510 derived from application No. 07/851,074 which was referred to on the cover page of WO '719.

The continued rejection over WO '719 is based on the presence of GGC and CGG motifs in the tables on pages 21 and 24. However, the tables are not present in Dean '510. Therefore, continued rejection of WO '719 does not carry over to Dean '510. The Lister-James declaration, submitted with the June 2003 response should be deemed sufficient to overcome the rejection based on Dean '510.

Rejection over Dean U.S. Patent No. 5,552,525

In paragraph 13 of the Office Action, the Examiner rejects all of the claims, except claims 3 and 20, under 35 U.S.C. § 102(e) as anticipated by Dean U.S. Patent No. 5,552,525 ("Dean '525").

> Claims 1, 2, 6-8, 11-17, 19, 21 and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean (U.S. Patent No. 5,552,525). Dean '525 teaches specific peptides in the Table at columns 10-11 which comprise a specific binding compound and a radiolabel complexing moiety. The peptides are labeled with Tc-99m, either through use of a stannous chloride reducing agent or through ligand exchange, and kits for preparing the radiolabeled peptides are provided (see, e.g., column 8, lines 21-65). The peptides are used to visualize sites of inflammation and infection (see, e.g., the Abstract and column 6, lines 52-62). With respect to the peptide, e.g., at claim 20 of Dean '525, the N-terminal residues CG correspond to a peptide comprising 2 amino acids attached to an amino group of Applicants' Y group, the residues CGG correspond to Applicants' radiolabel complexing moiety of formula II, and the remaining residues correspond to Applicants' radiolabel complexing moiety of formula II, and the remaining residues correspond toe Applicants' specific binding compound (see also claim 7 of Dean '525).

In their June 2003 response, Applicants argued that since Dean was the sole Applicant in the patent that matured into the Dean '525 reference, we do not have a "by another" situation which would be required in a proper rejection under 35 U.S.C. § 103(e). The Examiner rejected this contention, citing MPEP 2136.04.

In support of his rejection, the Examiner cites composition of matter shown in SEQ ID NO:4, in which the two cysteine residues are protected by acetamidomethyl (acm) groups. These cysteines are therefore not available for bonding. A further reason that the rejection under 35 U.S.C. § 102(e) is not valid is found in the Lister-James declaration that was submitted with the June 2003 response. In said declaration, Dr. Lister-James says that technetium binds preferably to a chelator presenting an –S-N-N-S- configuration rather than to a chelator having an –N-N-N-S- configuration. Thus, as stated in paragraph 11 of the declaration, in a peptide sequence such as –Gly-Gly-Cys-Gly-Cys-Gly-Gly- peptide, binding of technetium is most likely to occur with the –Cys-Gly-Cys- sequence, rather than to a possible –Gly-Gly-Cys- or –Cys-Gly-Gly- sequence. In Applicants' claimed reagents, the radiolabel complexing moiety has only a singe thiol group and therefore the structure in Dean '525 cited by the Examiner would not be a radiolabel complexing moiety within the scope of Applicants' claims.

Although the Lister-James Declaration was submitted primarily in order to overcome Dean U.S. Patent No. 5,561,220 and WO '719, the content of said declaration is equally applicable to Dean '525.

Rejection over Zamora U.S. Patent No. 5,556,609

In paragraph 14 of the Office Action, all of the claims, except claims 3 and 21, have rejected under 35 U.S.C. § 102(e) as anticipated by Zamora U.S. Patent No. 5,556,609 ("Zamora").

> Claims 1, 2, 6-8, 11-17, 19, 20 and 38 are rejected under 35 U.S.C. 102 (e) as being anticipated by Zamora (U.S. Patent No. 5,556,609). Zamora '609 teaches peptides

> comprising the sequence YIGSR, which targets cells containing receptors for YIGSR such as platelets which occur at thrombosis sites, and also comprising a metal ion-binding domain. See, e.g., the Abstract; column 4, lines 50-64; and column 7, lines 54-63. In Example 7, the metal ion-binding domain is CDG, which corresponds to Applicants' Formula I. In Example 7, the metal ion-binding domains are linked to the YIGSR sequences through one or more amino acids. The peptide in Example 7 labeled with Tc-99m in the presence of a stannous tartrate reducing agent. Labeling kits are also taught (see, e.g., column 7, lines 64-66). With respect to instant claim 13, process steps do not impart patentability to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

In the June 2003 response, Applicants pointed out that Zamora requires two biological function domains and two metal ion binding domains (equivalent to Applicants' "radiolabel complexing moieties", and that Applicants' claims are limited to reagents having only one specific binding compound and one radiolabel complexing moiety. In maintaining the rejection, the Examiner said

> The rejection based upon Zamora (U.S. patent No. 5,556,609) is maintained. Applicants distinguish Zamora on the basis that Zamora's compounds of example 7 contain two biological function domains and two metal ion-binding domains, whereas Applicants' claims are limited to reagents having one specific binding compound and one radiolabel complexing moiety. However, in order to demonstrate that Applicants' claims are limited to reagents having one specific binding compound and one radiolabel complexing moiety, Applicants point to indefinite articles found in the specification, whereas patentability must be based upon claimed differences over the prior art. The "comprising" language found in Applicants' claims, e.g., at claim 1, line 2, permits the presence of plural specific binding compounds and plural radiolabel complexing moieties.

Reconsideration is again requested.

Applicants respectfully traverse the Examiner's statement that the "comprising" language found in claim 1, line 2, would permit the presence of plural specific binding compounds and plural radiolabel complexing moieties. There is no support anywhere in the specification that would support this interpretation.

Rejections over WO 90/10463 and over WO 90/10463 in view of Fritzberg U.S. Patent No. 4,965,392

In paragraph 15 of the Office Action, the Examiner continues his rejections of claims 1-3, 6, 19 and 21 as anticipated by PCT publication WO 90/10463 ("WO'463").

> Claims 1-3, 6, 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 90/10463. The WO Patent Application '463 teaches reagents for and a method of imaging inflammation caused by infection. The reagents comprise a labeled recognition agent, where the recognition agent is capable of interacting selectively with activated leukocytes at the inflamed tissue sites. A preferred chelating compound for labeling the recognition agent is a N_3S metal chelating compound. A preferred recognition agent is a chemotactic peptide. The radiolabel can be Tc-99m. Also taught is a peptide recognition agent linked through a Gly_{1-5} spacer to a cysteine residue. Diagnostic kits including instructions for labeling are also taught. See e.g., the Abstract, page 3, lines 7-11, page 4, line 16 – page 5, line 21; page 7, lines 3-9; page 11, line 34 – page 13, line 3; page 26, line 16 – page 27, line 3; page 38, lines 28-35; page 39, line 26 – page 41, line 5, and claims 11, 12, 17, and 29-33.

In their June 2003 response, Applicants amended claim 1 and argued that WO '463 is not adequate as an anticipatory reference.

In paragraph 16 of the Office Action, the Examiner has rejected all of the claims, except claims 3 and 20, as obvious over WO '463 in view of Fritzberg U.S. Patent No. 4,965,392 ("Fritzberg")

> Claims 1, 2, 6-8, 11-17, 19, 21 and 38 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 90/10463 as applied against claims 1-3, 5, 6, 19, 21, and 34 above, and further in view of Fritzberg et al. (U.S. Patent No. 4,965,392). The WO Patent Application '463 does not teach a chemotactic peptide recognition agent labeled with N_3S metal chelating compound which is used to complex Tc-99m. Fritzberg et al. 392 teaches a N_3S metal chelating compound used to label a wide variety of polypeptide and carbohydrate compounds. Fritzberg et al. '392 preferred chelating compound is mercaptoacetylglycylglycylglycine, which is labeled with Tc-99m in the presence of a stannous ion reducing agent. See, e.g., column 6, line 35 – column 7, line 3, column 8, lines 24-29, and Examples I-IIIb, IV, and V. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the mercaptoacetylglycylglycylglycine chelating compound of Fritzberg et al. '392 to label the chemotactic peptide recognition agents of the WO Patent Application '463 because the mercaptoacetylglycylglycylglycine chelating compound of Fritzberg et al. '392 is a species of the N_3S metal chelating compounds generically disclosed by the WO Patent Application '463, because the mercaptoacetylglycylglycylglycine chelating compound of Fritzberg et al. '392 is disclosed as being useful in labeling a wide variety

> of polypeptide and carbohydrate compounds and therefore would have been expected to be useful in labeling the chemotactic peptide recognition agents of the WO Patent Application '463, because Fritzberg et al. '392 teach that their chelating compounds have the benefit of being able to accurately direct a radionuclide to a preselected site to reduce background radiation, to reduce dosage, to minimize background for in vivo imaging, and to minimize undesirable side effects (see column 1, lines 30-38), and because Fritzberg et al '392's chelating compound would permit labeling of the WO Patent Application '463's chemotactic peptide recognition agents with Tc-99m, which the WO Patent Application '463 discloses to be a useful radionuclide.

The substantially identical rejection was made in the December 2002 Office Action and Applicants argued, in part, that there would have been no motivation to combine the disclosures of WO '463 and Fritzberg.

Applicants' arguments with respect to both of these rejections were handled in a single response by the Examiner:

> The rejections based upon the WO Patent Application (90/10463 and upon the WO Patent Application 90/10463 in view of Fritzberg et al. (U.S. patent No. 4,965,392) are maintains. The WO Patent Application '463 does disclose reagents comprising two functionally distinct portions, namely a specific binding compound, i.e. the cognition agent which is bound to group Z at page 12, lines 22-24, and a radiolabel complexing moiety, i.e. the moiety having he structure at page 12, lines 1-10. Applicants discuss how the compound of Example 1 of the reference fails to anticipate the instant claims, with which discussion the examiner agrees. However, the disclosure of the reference is not limited to the single compound of Example 1, and Applicants have not explained how the sections of the reference actually relied upon by the examiner fail to anticipate the instant claims. Regardless of the disclosure at page 11, line 34 – page 13, line 3 of the WO Patent Application '463, the disclosure at page 38, lines 28-35 in and of itself anticipates the instant claims. This section of the reference teaches f-M-L-F-spacer-C where the spacer can be a chain of 1-5 glycines. Given the small number of species encompassed by the genus of 1-5 glycines, and given the specific naming of the endpoint of 5 glycines, one of ordinary skill in the art would immediately envisage chains of 3, 4 and 5 glycines. These compound f-M-L-F-spacer-C with a spacer of 3, 4 or 5 glycines has the same structure and function as Applicants' claimed reagents, and therefor anticipates Applicants' claimed reagents. Note that a mere difference in descriptive terminology does not impart patentability to Applicants' claims as long as the compound of the prior art has the same structure as Applicants' claimed compound. See In re Skoner, 186 USPQ 80, 82 (CCPA 1975). With respect to the obviousness rejection, the prior art suggestion or motivation to combine the references is et forth at page 18, lines 1-15, of the previous Office action and repeated above.

Reconsideration of both of these rejections is respectfully requested.

With respect to the anticipation rejection over WO '463, it is pointed out that, in order to constitute an adequate basis for such rejection, a single reference must unequivocally disclose the applicants' claimed invention. Example I of WO '463 discloses the preparation of the technetium labelled tetrapeptide fMLFC. It does not disclose a labelled reagent comprising "a specific binding compound that . . . comprises a peptide of from 4 to 100 amino acids" as required in Applicants' claim 1. WO '463 does not disclose a peptide covalently linked to an unlabeled radiolabel complexing moiety. Thus, Example V of WO '463 discloses conjugation between a peptide and a pre-labelled radiolabel complexing moiety (the LFC portion of the tetrapeptide of Example I. The passage pointed to by the Examiner – page 38, lines 28-35 – does not change the meaning of Examples I and V when read together. In these circumstances, WO '463 does not anticipate claims 1-3, 6, 19 and 21.

With respect to the obviousness rejection over WO '463 in combination with Fritzberg, Applicants again respectfully point out that this rejection is based on a hindsight analysis using Applicants' own specification. As noted in Applicants' Written Description – page 5, line 3 – Fritzberg describes certain chelators useful for labelling proteins. There is nothing in the Fritzberg reference about radiolabelling chemotactic peptide recognition units of the type disclosed in WO '463. The only possible way to connect these two references would be by a hindsight analysis using Applicants' specification because the disclosure of the primary reference is, in pertinent part, limited to chemotactic peptide recognition agents, while the disclosure of the secondary reference is concerned with proteins. We are dealing here with apples and oranges and, in these circumstances, the obviousness rejection is not tenable.

Rejection over the Plank Article

In paragraph 17 of the Office Action, claims 1-3, 6 and 19 have been rejected under 35 U.S.C. § 102(b) as anticipated by the previously-cited article by Plank et al.

> Claims 1-3, 6, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by the Plank et al article (Bioconj. Chem., Vol. 3, pages 533-539). The Plank et al article teaches compound 1B (Figure 1), in which the C-terminal Gly-Gly-Cys residues correspond to Applicants' radiolabel complexing moiety of formula I, and the N-terminal galacotside-polylysine-Gly residues correspond to Applicants' specific binding compound, and the remaining residues correspond alternatively to portions of Applicants' radiolabel complexing moiety, to Applicants' specific binding compound, or to the amino acids linking the peptide and the moiety. See also the Abstract.

In the June 2003 response, Applicants attempted to antedate this reference by pointing out that the anticipatory disclosure in the Plank reference, namely the amino acid sequence GRGDGGC, is identical to a sequence disclosed in Dean U.S. Patent No. 5,443,815, of which the instant application is a continuation-in-part. However, the Examiner did not accept this argument.

> The rejection based upon the Plank et al article (Bioconj. Chem., Vol. 3, pages 533-539) is maintained. As set forth in the effective filing date analysis in paragraph 5 above, Applicants' claims are not entitled to the benefit of the filing date of parent application 07/807,062. Accordingly, the Plank et al article is available as prior art against the instant claims under 35 U.S.C. 102(b). It is not possible to antedate a reference which is available as prior art under 35 U.S.C. 102(b). See 37 CFR 1.131(a)(2). If Applicants want their claims to be entitled to the benefit of the filing date of parent application 07/807,062, Applicants must limit the subject matter recited in the claims exclusively to that disclosed in the parent application. See, e.g., MPEP 201.11(VI) under "When Non Entitled To Benefit Of Filing Date", second paragraph.

Reconsideration of this rejection is respectfully requested, particularly in view of the foregoing proposed amendment to claim 1.

It is noted that claims 20 and 21, directed to reagents of claim 1 wherein the specific binding compounds bind respectively, to a thrombus site and to a site of an infection, were not included in this rejection. Thrombus sites and sites of an infection are examples of target sites in a mammalian body. Therefore, in order to differentiate

Applicants' claims from what is disclosed in the Plank reference, Applicants have proposed to amend claim 1 to specify that the specific binding compound binds to a target site in a mammalian body. Support for this amendment may be found in the Written Description at page 11, line 11.

Conclusion

Applicants submit that the foregoing amendment places all claims into condition for allowance. Therefore, it is believed that this amendment should be entered. However, even if the Examiner does not regard the claims as allowable, it is nevertheless requested that the Amendment be entered since it would place this application into better condition for appeal.

A Notice of Appeal accompanies this response.

Respectfully submitted,

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